

2. RESPONSE/REMARKS

2.1 STATUS OF THE CLAIMS

Claims 1-5 and 10-23 were pending at the time of the Action, and remain pending in the case.

2.2 REQUEST FOR CONTINUED EXAMINATION (RCE)

The present RCE is filed within the statutory six month period after the Final Action and is timely in light of the enclosed request for extension of time and fees.

2.3 THE OBJECTION TO CLAIMS 13 AND 14 WAS OVERCOME IN A PRIOR AMENDMENT.

Claims 13 and 14 remain objected to because of clarity. The Office has requested Applicants amend these claims to include “wherein said compounds have chemicals structures as follows:” language to improve their overall clarity.

Applicants respectfully traverse, and note for the record, however, that this rejection was previously addressed in the amendment and response dated September 11, 2008. In that amendment, Applicants incorporated the language previously suggested by the Examiner to remediate the perceived lack of clarity. Applicants now draw the Examiner’s attention to the accompanying submission, which includes the previously-amended language in claims 13 and 14 to address this objection.

Applicants respectfully assert that their previous amendment fully addresses the Office’s concern with respect to clarity, and respectfully request that the maintained objection be reconsidered and withdrawn.

2.4 THE FIRST REJECTION UNDER 35 U.S.C. § 103(A) IS OVERCOME.

Claims 1, 2, and 6-23 remain rejected under 35 U.S.C. § 103(a), allegedly as being obvious over Woodruff et al. (Arthr. and Rheum., 46:2476-85, 2002; hereinafter “Woodruff”) in view of Fairlie et al. (PCT Appl. Publ. No. WO 99/00406; hereinafter “Fairlie”) and Kivitz et al. (J. Fam. Prac., 51:530-7, 2002; hereinafter “Kivitz”).

The Action reiterates assertions made in the immediately prior Office Action that, because Woodruff teaches the use of AcF-[OPdChaWR] in the treatment of rheumatoid arthritis, it would also have been obvious to one of ordinary skill in the art at the time of the invention to utilize the C5a receptor antagonist (and related compounds) in a method for treating a distinctly different disease, *osteoarthritis*.

Although page 4 of the present Action clearly concedes that Woodruff does not teach the use of the claimed compounds to treat osteoarthritis, it is alleged that a “skilled artisan” would, nevertheless, “have been motivated to do so given the teaching of Kivitz et al. that pain and inflammation of rheumatoid arthritis and osteoarthritis patients can be treated with the same drugs, NSAIDs.” The Action continues that there “would have been a reasonable expectation of success given that Woodruff et al. teach that AcF-[OPdChaWR] can be used to treat inflammatory conditions.”

Again, Applicants respectfully renew their traversal of this rejection, initially because it applies the incorrect standard in that obviousness relates to that which one of *ordinary* skill would have been motivated to do, rather than what a *skilled* artisan would have been motivated to do.

To address the issue when first raised by the Office, Applicants previously submitted a third-party declaration by a well-known expert in the Applicants’ field of study that concluded the combination of the cited references would have been insufficient to motivate one of ordinary

skill in the art to attempt the treatment of osteoarthritis, with compounds that were previously shown to be effective in treating rheumatoid arthritis.

The present Action summarized particular passages from the first declaration submitted by the Applicants on pages 4 to 6, and concedes in the middle of page 6 three important points set forth in that first declaration:

- 1) “[O]steoarthritis and rheumatoid arthritis are fundamentally different diseases;”
- 2) “the fact that NSAIDs can be used to manage symptoms of both diseases is insufficient grounds for employing a C5a receptor antagonist known to treat rheumatoid arthritis to treat osteoarthritis;” and
- 3) “the role of the C5a receptor in osteoarthritis was not known in the prior art.”

As the Action concludes on page 6, “these arguments are persuasive and not contested.” Applicants appreciate the Examiner’s acceptance of the fundamental analysis set forth in Prof. Day’s first declaration.

However, the present Action maintains the earlier rejection of these claims, based upon an additional passage from Woodruff now excerpted in Section 15 of the present Action. This additional passage from Woodruff is said to “address[es] the limitations of NSAID and ibuprofen therapy for osteoarthritis, which as Applicant notes only treats the symptoms of the condition but not necessarily the underlying cause,” and is also said to “suggest that the cyclic peptide C5a receptor antagonist has additional effects over NSAIDs that are relevant to osteoarthritis. The fact that AcF-[OpdChaWR] moderates structural changes in the joint is reason to apply the compound to osteoarthritis even in the absence of information regarding the role of the C5a receptor in the disease.”

Applicants respectfully disagree with this conclusion, and traverse the additional rejection in view of the newly cited passage from Woodruff.

2.5 A SECOND DECLARATION UNDER 37 C.F.R. § 1.132 IS HEREBY PROVIDED.

The value of factual knowledge of those of ordinary skill in the art, as set forth in an affidavit or declaration, is well established under the law.¹ In *Katzschmann* (made in connection with overturning a rejection under 35 U. S. C. § 103[a]), the Court stated:

“We do not think it was the intent of § 103 that either the examiner, the Board or this Court should substitute their own speculations for the factual knowledge of those skilled in the art.”²

Therefore, even if the Office was held to have established a reasonable *prima facie* obviousness rejection, submission of an affidavit or declaration by a recognized third-party expert in the Applicants’ field of endeavor would be sufficient to overcome such a rejection.³

To that end, and to address the new rejection advanced over the cited combination of references, Applicants have provided a further declaration by Richard O. Day, Ph.D. pursuant to 37 C.F.R. § 1.132 (attached hereto as **Appendix A**, and containing three exhibits, labeled A to C, therein).

Applicants respectfully assert that this second declaration by Professor Day both addresses the Examiner’s concern, and effectively rebuts the obviousness rejection of the pending claims. As noted above, Dr. Day’s second declaration explains that, given the disclosures of Woodruff, Fairlie and Kivitz, it would have been highly improbable that a person of ordinary skill in the art intent on progressing research in a useful way would have been motivated by the collective teachings of these three references to develop a method for treating osteoarthritis using C5a receptor antagonists, and would certainly not have done so with the

¹ *In re Katzschmann*, 146 USPQ 66 (C.C.P.A. 1965); *In re Soni*, 34 USPQ2d 1684, 1688 (Fed. Cir. 1995).

² *Ibid.* 146 USPQ at 68.

³ *In re Katzschmann* and *In re Soni*, *supra*.

requisite expectation of success in achieving treating of such a disease as set forth in the pending claims.

In paragraph 4 of the second declaration by Dr. Day, he notes that although the Office has relied principally on the referenced paragraph to mainly support the present obviousness rejection, it is the Declarant's belief that the Office has misinterpreted the particular passage from Woodruff that is relied upon in the Final Office Action.

In paragraph 5 of the declaration, Prof. Day states that he does not believe that the single mention of osteoarthritis in the first sentence of this paragraph would lead “one of ordinary skill in the field of arthritis treatment to believe that a C5a antagonist had any role as a possible therapeutic in osteoarthritis.” He further supports this contention in paragraph 6 of the declaration, where he states that the Woodruff reference related to the use of C5a antagonist in the treatment of rheumatoid arthritis, which as the Office has previously conceded, is a separate disease that is unrelated to osteoarthritis. According to the Declarant, the model used in Woodruff “was a model of an antigen-induced monoarticular Arthus reaction”, which “produces a discrete lesion of highly reproducible severity in a single joint.” According to the Declarant, while the Woodruff teaching provides a model for *rheumatoid arthritis*, it would not have provided any predictive model for the treatment of osteoarthritis.

Paragraph 7 of the declaration further explains that, while IL-1 induced cartilage destruction is involved in both rheumatoid arthritis and osteoarthritis, the mechanism for IL-1 production is substantially different in the two disease processes. According to the Declarant, “it is not possible to simply extrapolate from a rheumatoid arthritis model to an osteoarthritis model, just as it is not possible to simply extrapolate the effective treatment of symptoms of rheumatoid arthritis to the treatment of the underlying etiology of osteoarthritis.”

Dr. Day continues his analysis of the present rejection by stating that he disagrees with the Examiner's conclusions that claimed invention is obvious in view of the cited art. According to the Declarant, the opening sentence of the paragraph of Woodruff relied upon by the Office is the only mention of osteoarthritis in the entire article. Paragraph 8 of the declaration states: “[t]his sentence reads: ‘[t]he destruction of cartilage in osteoarthritis results from the IL-1-stimulated degradation of proteoglycans and inhibition of chondrocyte proteoglycan synthesis (18).’”

As noted in Paragraph 9, the reference referred to as “18” in Woodruff is a paper authored by Wim B. van den Berg. The Declarant has attached a copy of the paper as **Exhibit A** to his declaration, and notes that the “van den Berg paper relates primarily to rheumatoid arthritis but does provide some discussion of the differences between osteoarthritis and rheumatoid arthritis in the final paragraph” that reads: “chondrocyte proteoglycan synthesis is suppressed in arthritis, but enhanced in OA.” The Declarant notes that he understands the reference to “arthritis” in the cited passage is to rheumatoid arthritis, while “OA” is understood to be osteoarthritis.

Importantly, in paragraph 10, Prof. Day notes “as opposed to providing support for the statement in Woodruff regarding osteoarthritis, van den Berg actually contradicts Woodruff,” and states that chondrocyte proteoglycan synthesis is *enhanced* in osteoarthritis, and not inhibited in osteoarthritis, as mentioned in the Woodruff reference. According to Dr. Day, “[c]hondrocyte proteoglycan synthesis is inhibited in rheumatoid arthritis not osteoarthritis.” **[Mark, doesn't this suggest the references teach away from each other? Why not say that explicitly here?]**

Paragraphs 11 and 12 of the second Day declaration submitted herewith note that the remainder of the paragraph cited in Woodruff “makes no mention of osteoarthritis,” and in his

view, the passage has nothing to do with the use of C5a antagonists in the treatment of osteoarthritis. According to Day, “[t]his passage is referring to the effects seen using a C5a antagonist in the model of rheumatoid arthritis used in Woodruff,” and any results obtained in the model of one disease “can not be extrapolated to the other disease.”

To support the Declarant’s opinion that the cited paragraph from Woodruff “has little or nothing to do with osteoarthritis,” Prof. Day attaches copies of two additional references cited by the Woodruff reference (denoted therein as reference “17” and reference “34”, and attached to the declaration as “**Exhibit B**” and “**Exhibit C**,” respectively), which are directed exclusively to rheumatoid arthritis, and “provide no information regarding osteoarthritis.” According to Prof. Day in paragraph 14 of his present declaration, “[t]he emphasis on rheumatoid arthritis in this paragraph is not surprising as this is the thrust of the entire paper.” According to Day, “the fleeting reference to osteoarthritis in the paragraph bridging pages 2483 and 2484 would not have provided a person of ordinary skill in the field of treatment of arthritis with any information regarding the possible use of a C5a antagonist in the treatment of osteoarthritis.”

More emphatically, the Declarant expresses his belief that “it is likely the person of ordinary skill would have simply ignored the reference to osteoarthritis as the paper does not provide any information regarding treatment of osteoarthritis or seen it is an error due to the mistaken reference to chondrocyte proteoglycan synthesis activity.” In paragraph 14, Dr. Day suggests “it is possible that the reference to ‘osteoarthritis’ should have been ‘rheumatoid arthritis’ as this would clearly fit with the remainder of the manuscript and the statement regarding chondrocyte proteoglycan synthesis activity.”

Prof. Day concludes his assessment that the cited combination of references would not have led one of ordinary skill in the art to develop the claimed methods for treating osteoarthritis, by stating in paragraph 15 of his declaration, “given that the models for rheumatoid arthritis and

osteoarthritis are different and that IL-1 induces cartilage destruction and the underlying mechanisms involved in IL-1 production in rheumatoid arthritis and osteoarthritis are believed to be different, I would not expect that a drug which reduces the degree of structural pathology in a model of rheumatoid arthritis to be effective in moderating structural changes in osteoarthritis.” Moreover, it is the Declarant’s opinion that he “would not expect that just because the C5a receptor antagonist AcF-[OPdChaWR] was shown by Woodruff to reduce the structural pathology in the joint of a rat model of rheumatoid arthritis, that… “[i]t would be similarly effective in treating the chronic joint degeneration associated with osteoarthritis.”

Therefore, in view of the Declarant’s opinion that the combination of references would *not* have rendered the claimed methods obvious, Applicants assert that a person of ordinary skill in the art would *not* have been motivated to combine the single disparate mention of “osteoarthritis” in the paragraph bridging pages 2483 and 2484 of Woodruff with any of the disclosures of Fairlie and/or Kivitz to achieve the claimed method for treating osteoarthritis using C5a antagonists, nor would one of such ordinary skill have had a reasonable expectation of success for achieving the claimed invention based upon the combination of references.

Moreover, Applicants respectfully maintain their assertion that the legal standard required for sustaining a rejection of the pending claims for obviousness over the three cited references *as a matter of law* has not been met. Furthermore, Applicants believe that the combination of Woodruff and the secondary references also fails to render the claimed invention obvious *as a matter of fact*. Thus, for the reasons set forth in the accompanying statement, and in those already of record, and discussed herein, Applicants respectfully request that the remaining obviousness rejection over the cited references be withdrawn.

2.6 THE SECOND OBVIOUSNESS REJECTION IS IMPROPER.

Claims 1-5 and 10-23 were also rejected under 35 U.S.C. § 103(a), allegedly as being obvious over Woodruff and Fairlie in further view of U. S. Patent 7,410,945 (hereinafter “the ‘945 patent”).

Applicants respectfully traverse.

Without acquiescing in any way to the propriety of the rejection, and without agreeing in any manner with the Office’s characterization of what the ‘945 patent does or does not “teach or suggest” or whether or not any aspects of the present invention is potentially rendered obvious by the reference, Applicants respectfully note for the record that (a) the ‘945 patent was commonly owned by the assignee of the present application at the time of invention of the above-captioned application; and (b) has at least one inventor in common with the present application.

Since this secondary reference could only constitute “prior art” under 35 U.S.C. § 102(e), Applicants respectfully note that even if the rejection is maintained over the combination of the reference with Woodruff, the rejection may still be overcome by showing that the ‘945 patent is disqualified as prior art under 35 U.S.C. § 103(c) in any rejection made with it under 35 U.S.C. § 103(a).

Applicants also further note that pursuant to M.P.E.P §§ 715.01(a), 715.01(c), 716.10, and 2136.05, an *In re Katz*-styled submission in accordance with 37 C.F.R. § 1.132 is also available to Applicants as a means for disqualifying the ‘945 patent as prior art if needed.

As noted in M.P.E.P. § 2136.05:

The fact that an application has named a different inventive entity than a patent does not necessarily make that patent prior art.” Applied Materials Inc. v. Gemini Research Corp., 835 F.2d 279, 15 USPQ2d 1816 (Fed. Cir. 1988). The issue turns on what the evidence of record shows as to who invented the subject matter. In re Whittle, 454 F.2d 1193, 1195, 172 USPQ 535, 537 (CCPA

1972). In fact, even if applicant's work was publicly disclosed prior to his or her application, applicant's own work may not be used against him or her unless there is a time bar under 35 U.S.C. 102(b). In re DeBaun, 687 F.2d 459, 214 USPQ 933 (CCPA 1982) (citing In re Katz, 687 F.2d 450, 215 USPQ 14 [CCPA 1982]). Therefore, when the unclaimed subject matter of a reference is applicant's own invention, applicant may overcome a *prima facie* case based on the patent, ** U.S. patent application publication>,< or international application publication, by showing that the disclosure is a description of applicant's own previous work. Such a showing can be made by proving that the patentee, or ** the inventor(s) of the U.S. patent application publication or the international application publication, was associated with applicant (e.g. worked for the same company) and learned of applicant's invention from applicant. In re Mathews, 408 F.2d 1393, 161 USPQ 276 (CCPA 1969).

When the reference reflects applicant's own work, applicant need not prove diligence or reduction to practice to establish that he or she invented the subject matter disclosed in the reference. A showing that the reference disclosure arose from applicant's work, coupled with a showing of conception by the applicant before the filing date of the reference will overcome the 35 USC 102(e) rejection. The showing can be made by submission of an affidavit by the inventor under 37 CFR 1.132. The other patentees need not submit an affidavit disclaiming inventorship, but, if submitted, a disclaimer by all other patentees should be considered by the examiner. In re DeBaun, 687 F.2d 459, 214 USPQ 933 (CCPA 1982).

Also relevantly, M.P.E.P. § 716.10 provides in pertinent part:

Under certain circumstances an affidavit or declaration may be submitted which attempts to attribute an activity, a reference or part of a reference to the applicant. If successful, the activity or the reference is no longer applicable. When subject matter, disclosed but not claimed in a patent application filed jointly by S and another, is claimed in a later application filed by S, the joint patent or joint patent application publication is a valid reference available as prior art under 35 U.S.C. § 102(a), (e), or (f) unless overcome by... an unequivocal declaration by S under 37 CFR § 1.132 that he or she conceived or invented the subject matter disclosed in the patent or published application. Disclaimer by the other patentee or other applicant of the published application should not be required but, if submitted, may be accepted by the examiner. (Emphasis added).

Applicants note that at the time the present invention was made, the inventors of the above-captioned application and the joint inventors named in the '945 patent each had common obligations of assignment to the assignee of record. Furthermore, Applicants submit that the '945 patent is subject to disqualification as prior art under 35 U.S.C. § 103 in view of subsection (c), which states:

(c) Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this Title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

As noted above, the instant application and the '945 patent were, at the time the invention of the present application was made, commonly owned, as evidenced by the assignments already of record with the Office. Therefore, under 35 U.S.C. § 103(c), the '945 patent should be disqualified as prior art under 35 U.S.C. § 103(a) against the claims of the present application. See, e.g., M.P.E.P. §§ 706.02(l)(1), 706.02(l)(2), and 2146.

Pursuant to 1241 O.G. 97 (December 26, 2000), which states, in pertinent part, that an Applicant or Applicant's attorney may, overcome such a rejection by "making a conspicuous statement that the application under examination and cited reference were commonly owned at the time the invention of the application under examination was made," In view of the fact that the instant and '888 applications are both assigned to Shell Oil, Applicant respectfully requests withdrawal of the present rejection for all pending claims.

To that end, Applicants respectfully assert that the '945 patent is not properly citable as prior art in a rejection under 35 U.S.C. § 103(a), because of its disqualification under 35 U.S.C. § 103(c), and as such, respectfully request that the rejection be withdrawn.

2.7 A TERMINAL DISCLAIMER MAY BE SUBMITTED TO OVERCOME REJECTION OF CLAIMS UNDER NON-STATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING.

The Office has rejected claims 1, 2 and 6-23 as allegedly being obvious for double patenting over claims 1-9 of the '945 patent in view of Woodruff and Fairlie.

The Office has also provisionally rejected claims 1, 2 and 6-23 as allegedly being obvious for double-patenting over the following claims further in view of Woodruff and Fairlie as detailed on pages 9 and 10 of the Action:

- a) claims 33-49 of copending application 12/193,943;
- b) claims 1-23 of copending application 12/144,266;
- c) claims 1-54 of copending application 12/045,088;
- d) claims 1-6, 8-10, 12, and 19-21 of copending application 10/493,117;
- e) claims 1-28 of copending application 10/531,565;
- f) claims 1-13 of copending application 11/807,651; and
- g) claims 1-28 of copending application 11/736,517.

Applicants respectfully traverse, and as noted above, respectfully argue that (as noted in the second declaration of Dr. Richard Day) the primary reference relied upon for the instant rejection (Woodruff) is irrelevant to the claimed methods of treating osteoarthritis, and as such, the addition of the various secondary references is insufficient to advance a rejection based upon obviousness. Because the secondary references relied upon cannot themselves form a sufficient basis for rejecting the pending claims, Applicants therefore believe that the cited provisional double-patenting rejections are rendered moot and should also now be withdrawn.

However, without acquiescing in any way to the merits of either the non-statutory obviousness-type double patenting over '945, or the provisional rejections over the cited pending applications, Applicants note for the record that even if their position that the reference by Woodruff is irrelevant to the claimed invention is unpersuasive, the submission of appropriate terminal disclaimers over the commonly-owned patent and patent applications would still be sufficient on their own to overcome *both* of these double-patenting rejections.

Applicants elect, however, to defer any such submission(s) until all other claim rejections have been withdrawn, and if needed an Examiner Interview has been conducted, following the Office's receipt and reconsideration of the rejections in view of the remarks herein and the content of the second declaration by Professor Day submitted herewith.

2.8 REQUEST FOR EXAMINER INTERVIEW

Pursuant to M.P.E.P. §§ 408, 713.01 and 713.09, and 37 C.F.R. § 1.133, Applicants hereby request an interview between Examiner Bradley and their undersigned representative to facilitate an expeditious conclusion of prosecution on the merits in the present application, and to permit expedited allowance and issuance of the pending claims prior to the issuance of any subsequent action on the merits.

Should any issues remain in the mind of the Examiner, or should any claims remain rejected for any reason following entry of the present submission, Applicants respectfully request that Examiner Bradley contact the undersigned representative to arrange a telephonic Examiner Interview at a mutually convenient time within the next thirty days, or before issuing any further Office Action other than a Notice of Allowance, to discuss favorable disposition of the case and the resolution of any remaining issues of record. Applicants appreciate in advance the Examiner's willingness to arrange such an interview, as noted in the teleconference conducted with the Office on June 5, 2009, should any issues concerning patentability of the pending claims remain following entry of the present submission including the second Declaration by Professor Day submitted herewith.

2.9 CONCLUSION

Applicants believe that all claims are acceptable under the Statutes and in condition for ready allowance. Applicants further believe that all of the Office's concerns have been fully addressed, and now earnestly solicit the withdrawal of all pending rejections, and the timely issuance of a Notice of Allowance.

Applicants reserve their right to re-file claims to one or more aspects of the invention as originally claimed in one or more continuing application(s) retaining the priority claim of the present application.

Should the Examiner have any questions upon entry of this response and consideration of the accompanying remarks, a telephone call to the Applicants' undersigned representative would be sincerely appreciated.

Respectfully submitted,



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June 11, 2009

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